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A BRIEF ORIGINAL CONTRIBUTION

Passive Smoking and Canine Lung Cancer Risk

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A case-control study was conducted to determine whether household exposure to environmental tobacco smoke is associated with an increased risk for lung cancer in pet dogs. Lung cancer cases and controls with other forms of cancer were obtained from two veterinary teaching hospitals during 1985–1987. Exposures assessed included the number of smokers in the household, the amount smoked, and the proportion of time spent indoors by the pet. A weak relation was found for exposure to a smoker in the home (odds ratio = 1.6, 95% confidence interval 0.7–3.7), after controlling for confounding in stratified analyses. Strong evidence for a further increase in risk associated with more than one smoker in the home was not found, nor was a significant trend observed for increasing number of packs of cigarettes smoked per day or an exposure index based on number of smokers in each household, packs smoked per day, and the proportion of time the dog spent within the home. However, skull shape appeared to exert effect modification; the risk was restricted to breeds with short and medium length noses (odds ratio = 2.4, 95% confidence interval 0.7–7.8). Despite the inconclusive findings of the current study, epidemiologic studies in pet animals may add to our understanding of environmental tobacco smoke effects in human populations. *Am J Epidemiol* 1992;135:234–9.

dogs; lung neoplasms; tobacco smoke pollution

Spontaneous canine neoplasms may provide useful models for studying the health effects of environmental hazards. Many forms of canine cancer resemble their human analogs in biologic behavior, pathologic expression, and recognized risk factors. Dogs share the environment intimately with humans, and thus they may constitute a "sentinel" species for human disease. Epidemiologic studies of environmental risk factors for cancer in pet dogs have been advocated because of the relative freedom from confounding factors such as occupational exposures and the dog's shorter life span and restricted residential mobility (1).

The relation between exposure to environmental tobacco smoke and the risk of human lung cancer and other, nonneoplastic respiratory diseases has received intense scrutiny from the scientific community, health policymakers, and others (2–6). The current study was designed to test the hypothesis that exposure to environmental tobacco smoke in the home constitutes a risk factor for lung cancer in dogs.

MATERIALS AND METHODS

All confirmed cases of canine lung cancer (n = 70) for the years 1985–1987 were se-

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Abbreviation: CI, confidence interval.

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lected from the oncology records systems of two university veterinary teaching hospitals (the University of Illinois and Colorado State University). Unmatched controls (n = 106) with other forms of cancer not suspected of being related to cigarette smoking in humans were selected randomly from the oncology data bases of the same institutions for the same years, yielding a case:control ratio of 1:1.5. The diagnoses of the primary lung cancer cases and cancer controls were verified histologically.

A letter soliciting participation was mailed to the household of each subject, with instructions to complete and return a questionnaire. Demographic information was collected for each participant. Exposures assessed among cases and controls included the number of smokers who resided in the household, the number of packs of cigarettes smoked per day by the heaviest smoker, and the proportion of time (per 24-hour day) spent by the dog inside the home. An exposure index was created for each subject by multiplying the number of smokers in each household by the number of packs smoked per day by the proportion of time the dog spent within the home. Thus, subjects that lived in homes where there was no resident smoker were assumed to have received no exposure.

Odds ratios with approximate 95 percent confidence intervals (7) were calculated to estimate risk. Mantel-Haenszel stratified analyses were used to control for confounding (8). The Mantel extension chi-square test was used to evaluate trends across strata of increasing dose (9).

Age, sex, hospital, proportion of the day spent indoors, body size, and skull shape were evaluated for confounding or effect modification. Body size (ideal weight for breed) could have influenced proximity to a smoking owner, as has been suggested for other human-canine exposures (10). It has been suggested that skull shape influences risk for respiratory cancer; long-nosed breeds have been shown to be at excess risk for nasal cancer in some studies (11, 12) but not in others (13). The suggestion that long nosed (dolichocephalic) breeds may more effectively filter and remove airborne particulates and carcinogens stimulated the inclusion of skull shape in stratified analyses.

RESULTS

The response rates were 73 percent for cases and 78 percent for controls, yielding final sample sizes of 51 and 83, respectively. Hospital A contributed 55 percent of the subjects—53 percent of the cases and 57 percent of the controls. Smoking was more prevalent among owners of dogs from hospital B, and therefore hospital was included as a potential confounder in all stratified analyses. The demographic and anatomic characteristics of lung cancer cases and other cancer controls were similar (table 1). The relative frequencies of various diagnoses among control dogs (table 2) were representative of all dogs with cancer as reported in other studies of university veterinary hospital populations (14).

A weak association was found between exposure to environmental tobacco smoke and the risk of canine lung cancer. The crude odds ratio for exposure to environmental smoke was 1.5 (95 percent confidence interval (CI) 0.7–3.0). After adjustment for age, sex, skull shape, time spent indoors, and hospital, the odds ratio rose slightly to 1.6

TABLE 1. Selected characteristics of case and control dogs from two veterinary medical teaching hospitals (the University of Illinois and Colorado State University), 1985–1987

Characteristic	Cases	Controls
No.	51	83
Mean age (years)	10.4	10.0
% male	47.1	50.6
Size (pounds)*		
Small (<25)	25.5	19.3
Medium (25–50)	35.3	41.0
Large (>50)	39.2	39.8
Skull shape		
Brachycephalic	5.9	6.0
Mesocephalic	47.1	49.4
Dolichocephalic	47.1	44.6

* To convert pounds to kilograms, multiply by 454 and divide by 1,000.

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(95 percent CI 0.7–3.7) (table 3). Effect modification by age appeared to be present; the risk estimate for dogs aged 10 years or less was 2.7 (95 percent CI 1.0–7.2), while that for older dogs was 0.8 (95 percent CI 0.3–2.2).

Evidence of a dose-response relation for passive smoke exposure was largely lacking (table 3). The risk estimate for more than one smoker in the home did not increase substantially over that found with a single smoker. Although the adjusted odds ratios for number of packs of cigarettes smoked daily by the heaviest smoker were in the anticipated direction for a dose response, the trend was not significant ($p = 0.20$). However, the total number of packs smoked in the home by all resident smokers could not be estimated from the data collected. When we evaluated an index of exposure that was calculated by multiplying number of smokers in the home, packs per day smoked by the heaviest smoker, and proportion of the day spent in the home by the dog, no in-

TABLE 2. Classification, by major diagnostic category, of control dogs from two veterinary medical teaching hospitals (the University of Illinois and Colorado State University), 1985–1987

Cancer site or type	No.	%
Breast	10	12.1
Soft tissue sarcoma	13	15.7
Skin and connective tissue	24	28.9
Gastrointestinal tract	9	10.8
Thyroid	5	6.0
Bone	6	7.2
Lymphoid	3	3.6
Other	13	15.7
Total	83	100.0

TABLE 3. Risk estimates for canine lung cancer by exposure to environmental tobacco smoke, University of Illinois and Colorado State University, 1985–1987

Risk factor	Cases exposed ($n = 51$)	Controls exposed ($n = 83$)	OR*, †	95% CI*
Presence of smoker in the home				
No smokers	27	52	1.0	
At least one smoker	24	31	1.6	0.7–3.7
No. of smokers in the home				
0	27	52	1.0	
1	16	17	1.6	0.6–4.1
≥2	8	14	1.8	0.4–7.1
-	(χ^2 for trend = 0.398; $p = 0.53$)			
Packs/day‡				
0	27	52	1.0	
<2	15	22	1.2	0.5–3.2
≥2	9	9	3.4	0.7–16.5
	(χ^2 for trend = 1.655; $p = 0.20$)			
Exposure index§				
0	27	52	1.0‖	
0.25–2.0	16	14	1.9‖	0.8–4.5
>2.0	8	17	0.9‖	0.3–2.9
	(χ^2 for trend = 0.123; $p = 0.73$)			

* OR, odds ratio; CI, confidence interval.
† Odds ratios were adjusted for age, sex, hospital, skull shape, and time spent indoors.
‡ No. of packs of cigarettes smoked per day by heaviest smoker.
§ No. of smokers × packs/day × percentage of time spent indoors.
‖ Not adjusted for time spent indoors.

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crease in risk was seen with presumed increases in exposure to environmental tobacco smoke (table 3).

Skull shape was found to exert a modifying effect on estimated lung cancer risk (table 4). The increase in risk for having a smoker in the home was restricted to members of breeds with short (brachycephalic) and medium length (mesocephalic) noses (odds ratio = 2.4, 95 percent CI 0.7–7.8), while no increase in risk was found in dogs with long noses. However, evidence of a dose-response relation was not found in the brachycephalic-mesocephalic group.

DISCUSSION

Primary canine lung cancer is a rare disorder, in terms of both proportional cancer mortality and prevalence. A prevalence ratio of 4.2 cases per 100,000 dogs was found in one population-based study (15). Lung cancers in dogs are primarily adenocarcinomas of bronchiolar and bronchioloalveolar origin which arise in the peripheral portions of the lung rather than in large airways (16).

Previous interest in canine lung diseases as models for human health effects has focused on the possible role of air pollution in chronic pulmonary disease (17) and in lung cancer (11). When the role of urban residence (a surrogate for air pollution exposure) was tested for its effect on the risk of canine pulmonary or nasal neoplasia, no relation was found (11). Environmental exposures to cigarette smoke were not considered in these analyses; an association between passive smoking and human lung cancer was not described until a decade later. In a recent epidemiologic study of bladder cancer in dogs, no association with exposure to environmental tobacco smoke was found (18).

The increase in risk found in this study in dogs corresponds reasonably well with the estimate of an increased risk for lung cancer

TABLE 4. Risk estimates for canine lung cancer by exposure to environmental tobacco smoke and by skull shape, University of Illinois and Colorado State University, 1985–1987

Risk factor	Brachycephalic/mesocephalic dogs				Dolichocephalic dogs			
	Cases exposed (n = 27)	Controls exposed (n = 46)	OR*, †	95% CI*	Cases exposed (n = 24)	Controls exposed (n = 37)	OR†	95% CI
Presence of smoker in the home								
No smokers	12	29	1.0		15	23	1.0	
At least one smoker	15	17	2.4	0.7–7.8	9	14	0.9	0.3–2.9
No. of smokers in the home								
0	12	29	1.0		15	23	1.0	
1	9	9	3.4	0.8–15.0	7	8	0.8	0.2–3.2
≥2	6	8	1.9	0.4–9.3	2	6	0.6	0.1–6.2
Packs/day‡								
0	12	29	1.0		15	23	1.0	
<2	10	11	2.5	0.6–10.0	5	11	0.7	0.2–2.5
≥2	5	6	2.4	0.4–13.1	4	3	2.1	0.2–25.3
Exposure index§								
0	12	29	1.0‖		15	23	1.0‖	
0.25–2.0	11	6	7.6‖	1.6–35.8	5	8	0.7‖	0.2–2.4
>2.0	4	11	1.2‖	0.2–5.4	4	6	0.6‖	0.1–4.0

* OR, odds ratio; CI, confidence interval.
† Odds ratios were adjusted for age, sex, hospital, and time spent indoors.
‡ No. of packs of cigarettes smoked per day by heaviest smoker.
§ No. of smokers × packs/day × percentage of time spent indoors.
‖ Not adjusted for time spent indoors.

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in humans of 1.35 that was calculated in a meta-analysis of the first 13 studies of lung cancer risk and passive smoking conducted worldwide (19). The current study suffers from some of the same limitations found in the studies done in humans, i.e, small sample sizes, imprecise risk estimates, and difficulties in measuring exposure.

Risk estimates in this study were stratified according to skull shape, because long-nosed breeds have been found to be at increased risk for nasal cancer in several epidemiologic studies (11, 12) and clinical reports (20). The suggestion that the increased risk of nasal cancer among dolichocephalic breeds may be due to enhanced filtration of airborne particulates and carcinogens led us to examine the relation between skull shape and lung cancer risk. The finding that increased canine lung cancer risk is restricted to dogs with short and medium length noses (brachycephalic and mesocephalic breeds) is consistent with the hypothesis that the relatively efficient air filtration of the long-nosed breeds may exert a protective effect for lung cancer. Experimental attempts to induce lung cancer in dogs by exposing them to cigarette smoke proved successful when the nasal filtration mechanism was bypassed by exposing the animals through a tracheostomy (21). Over 40 percent of dogs that "smoked" unfiltered cigarettes for up to 2½ years developed lesions classified as invasive bronchioloalveolar tumors (21). Furthermore, the low incidence of lung cancer in dogs may be partly attributable to effective filtration of inspired air within the nasal cavity and turbinates.

Use of the dog model has several advantages over comparable studies in humans in that exposures are largely restricted to the home, and potential confounding by occupational exposures to other airborne carcinogens is reduced. Nonetheless, while the dog's mobility is restricted, that of its smoking owner(s) is not, and it becomes difficult to ascertain exposure precisely. In the current study, the proportion of total smoking conducted in the home (as opposed to other sites) was not determined, and information on number of packs currently smoked per day was collected only for the heaviest smoker in the home. Duration of exposure was not evaluated, although it may also be relevant, since the induction time for lung cancer is likely to be measured in years. Thus, misclassification with respect to dose undoubtedly occurred and may have obscured differences between exposure groups. Recent studies in humans have emphasized the importance of childhood and adolescent exposures to environmental tobacco smoke in the household as determinants of the risk of lung cancer (6).

Hospital-based case-control studies may suffer from selection bias. However, in this study, there is no reason to suspect differential referral patterns from smoking and nonsmoking families, and cancer controls were chosen to minimize this possibility. Furthermore, the selection of cancer controls was intended to reduce the information bias that may result from differential recall of exposure among owners of case and control dogs (22).

The rarity of lung cancer in dogs makes a collaborative multicenter case control study the design of choice for further studies of canine lung cancer. Studies of nasal cancer, a more common form of cancer in dogs, are under way to examine the effects of environmental tobacco smoke on the nasal epithelium. Demonstration of an association between exposure to environmental tobacco smoke and canine respiratory cancer would provide additional evidence with which to evaluate this important public health concern.

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